AF/1635 #8 BP 9-5-01

BEFORE THE BOARD OF APPEALS AND INTERFERENCES
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Chaudhary

Serial No. 09/490,187

Filed: January 23, 2000

For: *Gene Expression in Ectodermal Dysplasia*

Group Art Unit: 1635

Examiner: McGarry, S.

Attorney Docket No. UTSD:0680

CERTIFICATE OF MAILING
I hereby certify that this corr. is being deposited with the US Postal Service as First Class Mail in an envelope addressed to the Comm. for Patents, Washington, D.C. 20231 on August 27, 2001.

Signed _____
Richard Osman

BRIEF ON APPEAL

The Honorable Board of Appeals and Interferences
United States Patent and Trademark Office
Washington, D.C. 20231

Dear Honorable Board:

This is an appeal from the March 28, 2001 Final Action.

REAL PARTY IN INTEREST

The real party in interest is Board of Regents, The University of Texas System, the assignee of this patent application.

RELATED APPEALS AND INTERFERENCES

Appellants are unaware of any related appeals or interferences.

STATUS OF THE CLAIMS

Claims 1-21 are pending and subject to this appeal.

STATUS OF THE AMENDMENTS

All Amendments are believed to be properly before the Board.

SUMMARY OF THE INVENTION

The ectodermal dysplasia syndromes are a group of genetic disorders which are identified by the absent or deficient function of derivatives of ectoderm (e.g. skin, nail, sweat glands or teeth). At least 150 different syndromes have been identified and it is estimated that the incidence of these disorders may be as high as 7 per 10,000 births. Two major subgroups of ectodermal dysplasias are hypohidrotic ectodermal dysplasia (HED) and hidrotic ectodermal dysplasia or Clouston syndrome (Ellis et al., 1980, Clin Exp Dermatol 5, 295-304; Pinheiro et al., 1994, Am J Med Genet 53, 153-162; Kere et al., 1997, US Pat No.5,700,926). Specification, p.1, lines 11 - 17.

Mutations in the human homolog of mouse *dl* have recently been reported to cause autosomal recessive and dominant hypohidrotic ectodermal dysplasia (Monreal, et al. 1999 Nature Gen 22, 366-369; Headon et al. 1999 Nature Gen 22, 370-374. We previously isolated a new member of the TNFR family, designated TAJ (originally, APO4, Chaudhary, 1999, WO9911791) and characterized its expression in embryonic and prostate tissue. Here we disclose that TAJ may be exploited for post and pre-natal diagnosis and treatment of ectodermal disorders such as Clouston syndrome. Specification, p.1, lines18 - 24.

The invention provides methods and compositions for diagnosing and treating ectodermal disorders associated with misexpression of a TAJ gene. In one embodiment, the invention provides methods of detecting the presence of or predisposition to an ectodermal disorder comprising the steps of (a) detecting the presence of a TAJ gene or gene product in a cell; and (b) correlating the presence of the TAJ gene or gene product with a presence of or predisposition to an ectodermal disorder. The detection may be direct, indirect or inferential and at the level of the TAJ gene, transcript, protein or any intermediate processing stage. In particular embodiments, the detecting step is performed inferentially by determining a diagnostic sequence of the TAJ gene or gene product in the individual; the TAJ gene or gene product is a variant correlated with the presence of or predisposition to an ectodermal disorder; the ectodermal disorder is an

ectodermal dysplasia syndrome, such as Clouston syndrome. Specification, p.1, line 27 - p.2, line 7.

In another embodiment, the invention provides a method for modulating the functional expression of a TAJ gene or gene product in a cell comprising the step(s) of contacting a cell with an agent which specifically binds and modulates the functional expression of a TAJ gene or gene product, wherein (a) the cell is an ectodermal cell; or (b) the cell is a pluripotent cell which is capable of giving rise to progeny ectodermal cells and detecting the functional expression of the TAJ gene or gene product in the progeny cells. In particular embodiments, the cell is in situ or ex situ, the contacting step reduces or increases the functional expression of the TAJ gene or gene product, the agent is an antibody or intrabody which specifically binds a TAJ protein; the agent is an agonist or antagonist of a TAJ protein; the agent is an antisense oligonucleotide which specifically binds a TAJ gene transcript; the agent is an oligonucleotide which specifically binds a TAJ gene, etc. In more particular embodiments, the agent is an oligonucleotide which specifically binds a TAJ gene, whereby the gene is changed to a different TAJ gene, particularly whereby the gene is changed from a TAJ gene correlated with a presence of or predisposition to an ectodermal disorder to a different TAJ gene not so correlated, particularly wherein the ectodermal disorder is an ectodermal dysplasia syndrome, such as Clouston syndrome. Specification, p.2, lines 8 - 23.

ISSUE

I. WHETHER CLAIMS 1-21 ARE PATENTABLE UNDER THE ENABLEMENT REQUIREMENT OF 35USC112, FIRST PARAGRAPH.

GROUPING OF THE CLAIMS

Claims 1-2 and 4-5 shall stand as a group; claim 3 shall stand separately; claim 6 shall stand separately; claim 7 shall stand separately; claim 8 shall stand separately; claims 9-13 and 15 shall stand as a group; claim 14 shall stand separately; claim 16 shall stand separately; claim 17 shall stand separately; claim 18 shall stand separately; claim 19 shall stand separately; claim 20 shall stand separately; and claim 21 shall stand separately.

ARGUMENT

I. CLAIMS 1-21 ARE PATENTABLE UNDER THE ENABLEMENT REQUIREMENT OF 35USC112, FIRST PARAGRAPH.

Claims 1-8 require detecting the presence of or predisposition to an ectodermal disorder by (a) detecting the presence of a human TAJ gene or gene product in a cell; and (b) correlating the presence of the TAJ gene or gene product with a presence of or predisposition to an ectodermal disorder.

The Specification thoroughly teaches and exemplifies the method defined by these steps, readily enabling one of ordinary skill in the art to practice the method as claimed without undue experimentation. For step (a), the Specification describes a variety of suitable detection methodologies (p.4, lines 9-28; p.6, lines 3-13), teaches a large panel of exemplary TAJ specific probes (allele-specific antibodies and hybridization probes; p.4, line 31 - p.6, line 2), and provides detailed exemplification of detection by in situ and chromosomal hybridization (p.9, lines 3-17), TAJ allele-specific PCR amplification (p.12, lines 5-22), transcriptional reporter assay (p.10, lines 6-29), and immunocytochemistry (p.14, line 29 - p.15, line 5); see also p.17, lines 14-31. Step (b) involves no more than correlating the detected TAJ gene or gene product with an ectodermal disorder. In many cases, this entails no more than cross-referencing to a known clinical correlate. The Specification describes alternative means to implement this step (p.6, lines 14-26), teaches a large panel of TAJ genes and gene products associated with an ectodermal disorder (p.3, line 16 - p.4, line 3) and provides detailed exemplification of correlation by chromosomal mapping (p.9, lines 12-17), animal model (p.9, line 18 - p.10, line 3) and clinical diagnosis (p.12, lines 5-22).

Both required steps of these TAJ detecting claims are thoroughly taught, described and exemplified, fully enabling one skilled in the art to practice the claimed invention without undue experimentation. The Action's criticisms of the TAJ detection data reported in the Specification, and particularly the reporting of qualitative as opposed to quantitative data, are believed to reside outside the bounds of a proper enablement analysis duly limited to the recited claims. For example, Table 2 provides exemplary allele-specific TAJ antibodies and allele-specific hybridization probes. Rather than reciting quantitative data that cannot be compared across

experiments, the Table indicates demonstrable allele-specific antibody binding with a normalizing "+++" designation, and demonstrable allele-specific hybridization with a "+++" designation. The qualitative "+++" indicates that unequivocal allele-specific binding or allele-specific hybridization is obtained. Specific-binding/hybridization are readily assayed by those skilled in the art, and exemplified in our Specification, e.g. Examples III and IV. Similarly, we believe the Action's statements regarding the correlation step presume that the claims require more than the recited step. Note that the entire detection method is exemplified in Example IV, wherein the practitioner detects the presence of the human TAJ gene product (by PCR) and correlates that presence with an ectodermal disorder (Clouston syndrome).

The Action's suggestion that correlating the many ectodermal disorders that may be associated with TAJ mutations would involve undue trial and error appears to read too much into the required claim step. Our claims do not require correlating every ectodermal dysplasia with every TAJ mutation, but merely detecting *a* TAJ mutant and then correlating *that* mutant to the presence of *an* ectodermal disorder. Whether the number and potential causes of ectodermal disorders are 5 or 500 is submitted to be not relevant to our claims. Note, for example, the exemplification shown in Example IV (p.12, lines 5-22). There is no trial and error – the cell comes from a particular source (e.g. patient) having a particular clinical presentation, to which the practitioner is not blind. In fact, a particular clinical presentation of ectodermal disease is the reason the patient's TAJ gene is being analyzed. In *In re Wands*, the enablement issue was not whether it would require undue experimentation to make all the possible antibodies having the required affinity, but rather whether it would require undue experimentation to make a given such antibody. Similarly, here the issue is not whether it would require undue experimentation to analyze the correlation of every possible TAJ mutant with every possible ectodermal disorder, but rather whether it would require undue experimentation to analyze the correlation of *a* TAJ mutant to *an* ectodermal disorder - and one single disorder will suffice for our claims.

Though there is no evidence to the contrary, we have provided an expert Declaration under 37CFR1.132 documenting that the Specification readily enables one of ordinary skill in the art to practice this two-step detection method as claimed without undue experimentation.

Claim 3 further requires that the detecting step comprises detecting a TAJ gene transcript.

As detecting a TAJ gene transcript is the particular detection method exemplified in Example IV, this claim is further removed from the enablement rejection.

Claim 6 further requires that the TAJ gene or gene product is a variant correlated with the presence of or predisposition to an ectodermal disorder. As this claim is limited to mutants previously correlated with an ectodermal disorder, this correlation is inherent in the patient's history. This invention avoids any effort to identify the correlate and is further removed from the enablement rejection.

Claim 7 further requires that the ectodermal disorder is an ectodermal dysplasia syndrome. As this claim is limited to detecting a more narrowly defined ectodermal disorder having a particularly exemplified species (see, e.g. Example IV) correlated with particular TAJ mutants, it is further removed from the enablement rejection.

Claim 8 further requires that the ectodermal disorder is an ectodermal dysplasia syndrome and the syndrome is Clouston syndrome. As this claim is limited to detecting a particularly exemplified ectodermal disorder (see, e.g. Example IV) correlated with particular TAJ mutants, it is further removed from the enablement rejection.

Claims 9-21 require modulating the functional expression of a TAJ gene or gene product in a cell by contacting the cell with an agent which specifically binds and modulates the functional expression of a human TAJ gene or gene product, wherein (a) the cell is an ectodermal cell; or (b) the cell is a germ cell which gives rise to progeny ectodermal cells and further detecting the functional expression of the TAJ gene or gene product in the progeny cells.

The Specification thoroughly teaches and exemplifies the method defined by these steps, readily enabling one of ordinary skill in the art to practice the method as claimed without undue experimentation. The Specification explains how this method is implemented, including its application to germ cells which give rise to progeny ectodermal cells (p.6, line 29 - p.7, line 9), describes a variety of suitable TAJ binding and modulatory agents (p.7, lines 10-19), teaches a panel of exemplary agents shown to allele-specifically modulate functional expression of a TAJ gene or gene product (p.7, line 21 - p.8, line 18), describes how these agents are delivered to the cell (p.8, lines 20-30), and provides detailed exemplification of the method as applied to human keratinocytes in vitro and in vivo (Examples V and VI, p.12, line 24 - p.17, line 31).

The required step(s) of the TAJ modulating claims are thoroughly taught, described and exemplified, fully enabling one skilled in the art to practice the claimed invention without undue experimentation. The Action's criticisms of the data reported in the application, and particularly the reporting of qualitative as opposed to quantitative data, are believed to reside outside the bounds of a proper enablement analysis duly limited to the recited claims. For example, Table 3 provides exemplary agents which allele-specifically modulate TAJ expression. Rather than reciting quantitative data that cannot be compared across experiments, the Table indicates demonstrable allele-specific expression modulation with a normalizing "+++" designation. The qualitative "+++" indicates that unequivocal allele-specific expression modulation is obtained. Changes in TAJ expression are readily assayed by those skilled in the art, as taught and exemplified in our Specification, e.g. Example VI. Similarly, we believe the Action's statement that the claims include methods of treating any TAJ disorder is not properly confined to the invention recited in our claims. Note that the entirety of the claimed modulating method is exemplified in Example VI.

Though there is no evidence to the contrary, we have provided an expert Declaration under 37CFR1.132 documenting that the Specification readily enables one of ordinary skill in the art to practice this modulation method as claimed without undue experimentation.

Claim 14 further requires that the agent is an intrabody which specifically binds a TAJ protein. As this claim is limited to use of a particularly exemplified binding agent (see, e.g. Specification, p.8, lines 7-12) shown to modulate the functional expression of a TAJ gene product, it is further removed from the enablement rejection.

Claim 16 further requires that the agent is an antisense oligonucleotide which specifically binds a TAJ gene transcript. As this claim is limited to use of a particularly exemplified binding agent (see, e.g. Specification, p.8, lines 13-18) shown to modulate the functional expression of a TAJ gene product, it is further removed from the enablement rejection.

Claim 17 further requires that the agent is an oligonucleotide which specifically binds a TAJ gene. As this claim is limited to use of a particularly exemplified binding agent (see, e.g. Specification, p.7, line 26 - p.8, line 6) shown to modulate the functional expression of a TAJ gene, it is further removed from the enablement rejection.

Claim 18 further requires that the agent is an oligonucleotide which specifically binds a TAJ gene, whereby the gene is changed to a different TAJ gene. As this claim is limited to use of a particularly exemplified binding agent (see, e.g. Specification, p.7, line 26 - p.8, line 6) shown to modulate the functional expression of a TAJ gene, and further exemplified in experimental detail (Example VI), it is further removed from the enablement rejection.

Claim 19 further requires that the agent is an oligonucleotide which specifically binds a TAJ gene, whereby the gene is changed from a TAJ gene correlated with a presence of or predisposition to an ectodermal disorder to a different TAJ gene not so correlated. As this claim is limited to use of a particularly exemplified binding agent (see, e.g. Specification, p.7, line 26 - p.8, line 6) shown to modulate the functional expression of a TAJ gene, and even further limited to an embodiment exemplified in experimental detail (Example VI), it is further removed from the enablement rejection.

Claim 20 further requires that the agent is an oligonucleotide which specifically binds a TAJ gene, whereby the gene is changed from a TAJ gene correlated with a presence of or predisposition to an ectodermal disorder to a different TAJ gene not so correlated, wherein the ectodermal disorder is an ectodermal dysplasia syndrome. As this claim is limited to use of a particularly exemplified binding agent (see, e.g. Specification, p.7, line 26 - p.8, line 6) shown to modulate the functional expression of a TAJ gene, and even further limited to an embodiment exemplified in experimental detail (Example VI), it is further removed from the enablement rejection.

Claim 21 further requires that the agent is an oligonucleotide which specifically binds a TAJ gene, whereby the gene is changed from a TAJ gene correlated with a presence of or predisposition to an ectodermal disorder to a different TAJ gene not so correlated, wherein the ectodermal disorder is an ectodermal dysplasia syndrome and the syndrome is Clouston syndrome. As this claim is limited to use of a particularly exemplified binding agent (see, e.g. Specification, p.7, line 26 - p.8, line 6) shown to modulate the functional expression of a TAJ gene, and even further limited to an embodiment exemplified in experimental detail (Example VI), it is further removed from the enablement rejection.

Appellants respectfully request reversal of the pending Final Action by the Board of Appeals.

Appellants hereby petition for any necessary extension of time pursuant to 37 CFR 1.136(a). The Commissioner is hereby authorized to charge any necessary fees associated with this communication to our Deposit Account No. 19-0750 (order no. UTSD:0680).

Respectfully submitted,
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encl. 132 Declaration (3 pg, of record)

CLAIMS ON APPEAL

1. A method for detecting the presence of or predisposition to an ectodermal disorder comprising the steps of:

(a) detecting the presence of a human TAJ gene or gene product in a cell; and

(b) correlating the presence of the TAJ gene or gene product with a presence of or predisposition to an ectodermal disorder.

2. The method according to claim 1, wherein the detecting step comprises detecting a TAJ gene.

3. The method according to claim 1, wherein the detecting step comprises detecting a TAJ gene transcript.

4. The method according to claim 1, wherein the detecting step comprises detecting a TAJ protein.

5. The method according to claim 1, wherein the detecting step is performed inferentially by determining a diagnostic sequence of the TAJ gene or gene product in the individual.

6. The method according to claim 1, wherein the TAJ gene or gene product is a variant correlated with the presence of or predisposition to an ectodermal disorder.

7. The method according to claim 1, wherein the ectodermal disorder is an ectodermal dysplasia syndrome.

8. The method according to claim 1, wherein the ectodermal disorder is an ectodermal dysplasia syndrome and the syndrome is Clouston syndrome.

9. A method for modulating the functional expression of a TAJ gene or gene product in a cell comprising the step(s) of:

contacting a cell with an agent which specifically binds and modulates the functional expression of a human TAJ gene or gene product, wherein:

(a) the cell is an ectodermal cell; or

(b) the cell is a germ cell which gives rise to progeny ectodermal cells and the method further comprises the step of detecting the functional expression of the TAJ gene or gene product in the progeny cells.

10. The method according to claim 9, wherein the cell is in situ.

11. The method according to claim 9, wherein the cell is ex situ.

12. The method according to claim 9, wherein the contacting step reduces the functional expression of the TAJ gene or gene product.

13. The method according to claim 9, wherein the agent is an antibody which specifically binds a TAJ protein.

14. The method according to claim 9, wherein the agent is an intrabody which specifically binds a TAJ protein.

15. The method according to claim 9, wherein the agent is an agonist or antagonist of a TAJ protein.

16. The method according to claim 9, wherein the agent is an antisense oligonucleotide which specifically binds a TAJ gene transcript.

17. The method according to claim 9, wherein the agent is an oligonucleotide which specifically binds a TAJ gene.

18. The method according to claim 9, wherein the agent is an oligonucleotide which specifically binds a TAJ gene, whereby the gene is changed to a different TAJ gene.

19. The method according to claim 9, wherein the agent is an oligonucleotide which specifically binds a TAJ gene, whereby the gene is changed from a TAJ gene correlated with a presence of or predisposition to an ectodermal disorder to a different TAJ gene not so correlated.

20. The method according to claim 9, wherein the agent is an oligonucleotide which specifically binds a TAJ gene, whereby the gene is changed from a TAJ gene correlated with a presence of or predisposition to an ectodermal disorder to a different TAJ gene not so correlated, wherein the ectodermal disorder is an ectodermal dysplasia syndrome.

21. The method according to claim 9, wherein the agent is an oligonucleotide which specifically binds a TAJ gene, whereby the gene is changed from a TAJ gene correlated with a presence of or predisposition to an ectodermal disorder to a different TAJ gene not so correlated, wherein the ectodermal disorder is an ectodermal dysplasia syndrome and the syndrome is Clouston syndrome.